Serological clusters in inflammatory myositis and its clinical and prognostic implications: a longitudinal cohort study

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ABSTRACT

Objective. *Clinicoserologic inflammatory myopathies (IM) classification has revolutionised the diagnostic approach to this heterogeneous disease entity. The objective of this study was to determine the subgroups predictive prognostic factors that formed after a population cluster analysis.*

Methods. *Prospective multicentre study of 108 subjects with myositis. An ascending hierarchical classification (AHC) was carried out on the axes of a multiple correspondence analysis (MCA) to group individuals into homogeneous clusters. Prognostic predictors were identified using binary logistic regression. "R" software was used in the statistical analysis.*

Results. *82 patients were women (75.9%), aged 50.4±14.7. Patients were split according to clinical and immunological data of those with: antisynthetase syndrome (ASS) 34 (38.6%), dermatomyositis (DM) 31 (28.7%), overlap myositis (OM) 27(30.7%), seronegative myositis 8 (7.4%), immune-mediated necrotising myositis (IMNM) 6 (6.8%) and inclusion body myositis (IBM) 2 (2.3%). MCA analysis differentiates three clusters: Cluster 1 (n=27) including OM patients characterised by dysphagia, creatine kinase (CK) level >225 with very few men. Cluster 2 (n=34) included ASS patients, mainly men (<50 years), smokers, with arthritis and cytoplasmic ANA. Cluster 3 (n=31) included DM patients aged ≥50 years having strength limitation (MMT8 ≤ 3) contrasting with low CK level with typical skin involvement. Second line IS use (OR=4.3; 95% CI 1.55–12.49) and cytoplasmic ANA (OR=4 .4; 95% CI 1.64–12.61) was ASS predictive; MMT8 ≤3 (OR=4.5; 95% CI 1.58–14.46) was DM predictive and dysphagia (OR=3.55; 95% CI 1.13–12.17), diagnostic delay (OR=3.41; 95% CI 1.17–10.32) were OM predictive.*

Conclusion. *Antibodies in myositis has a double diagnostic and prognostic interest and each cluster is fairly well defined by specific prognosis predictive factors.*

Introduction

Inflammatory myopathies (IM) are a group of rare, acquired autoimmune diseases, sometimes leading to diagnostic and therapeutic delays. Incidence of these pathologies is about 8.22/million inhabitants/year (1). The definition of this disease is based on the characterisation in the patient of skeletal muscle manifestations secondary to an immune response (serological and histological) and/or extra-muscular involvements. The diagnosis is clinically based on a rigorous anamnesis, electromyography data and an assessment looking for myositis-specific antibodies (MSA). Indeed, diagnosis was formerly based strictly on the results of muscle biopsy, but since the advent of MSA, homogeneous subgroups of patients with specific phenotype and prognosis have been isolated. These include dermatomyositis (DM), antisynthetase syndrome (ASS), overlap myositis (OM), immune-mediated necrotising myopathy (IMNM) and inclusion body myositis (IBM) (2). Through this multicentre research work, we divided 108 Algerian IM patients into clusters using an analysis inspired by studies made using the the last classification but also the ACR/EULAR 2017 criteria (3, 4) and we determined the predictive factors of each cluster. This work will ultimately lead to proposing a simplified regional algorithm to

facilitate the diagnosis and therapeutic strategy for IM patients.

Patients and methods

Methods of statistical analysis

This prospective, descriptive multicentre longitudinal study was carried out on 108 Algerian IM patients. IM was classified and defined according to the 2017 ACR/EULAR criteria (3). R software was used in the statistical analysis (v. 4.4.1 manufactured by Austria). Descriptive statistics were used to represent study variables. Multiple correspondence analysis (MCA) was carried out taking into account all characteristics. An ascending hierarchical classification (CAH) was achieved using the coordinates of the subjects on the MCA axes in order to group patients into homogeneous clusters. To identify the prognostic factors of the clusters, binary logistic regression was applied (univariate analysis *p*-value <0.15). The study was conducted in accordance with the declaration of Helsinki. The study was approved by the ethics committee and informed consent was signed by all patients before the start of the study.

Results

Overview of study population

The main data characteristics of the study population are illustrated in Table I. Distribution into IM subgroups is shown in the pie chart (Fig. 1). Based on clinical data and MSA, we were able to divide our cohort into 34 (31.5%) ASS, 31 (28.7%) DM, 27 (25%) OM, 8 (7.4%) IM seronegative, IMNM 6 (5.5%) and IBM 2 (1.8%) (Fig. 1).

Other more detailed parameters were collected: 22 (20.8%) were diabetic, smokers in 9 (8.3%). 46 (42.6%) had DXA scan, osteoporosis was found in 23 (54.76%) (45% were started on treatment). The diagnostic delay was 23.6 months ± 38.3. All the patients had muscle involvement, creatine kinase (CK) levels were positive in 43 (41%) and electromyography tracing was myogenic in 87 (81.3%). DAS28 was ≤2.6: 36 (33.3%), 2.6<DAS28≤3.2: 28 (25.9%) or low activity, 3.2<DAS≤5.1: 41 (38%) or moderate activity, DAS>5.1: 3 (2.8%) or high activity.

Table I. Principal characteristics of study population.

Characteristics	Frequencies (%)
Average age (years)	50.4 ± 14.7
Women	82 (75.9)
BMI	24.4 ± 4.5
HBP	33 (31.1)
Dyslipidaemia	19 (17.9)
Statins	9 (8.4)
Dysthyroidism	38 (35.5)
Motor signs	107 (100)
Joint damage	90 (83.3)
NTJ	6.1 ± 4.4
NSJ	0.3 ± 0.9
Skin damage	55 (50.9)
Respiratory impairment	66 (61.1)
Raynaud	88 (82.2)
Dysphagia	35 (32.5)
Associated cancer	3 (2.8)
ESR	31.9 ± 29.2
CRP	12.7 ± 35.4
Creatine kinase	1176.7 ± 2997.8
Pattern scan	
Normal	42 (40.18)
NSIP	34 (51.5)
IUP	11 (16.6)
NSIP/OP	9 (13.63)
others	12 (18.27)
PFT	
≥70%	75 (73.5)
<70%	27 (26.5)
Capillaroscopy	
Normal	10 (10.10)
NSM	42 (47.2)
SM	47 (71.29)
ANA	77 (71.29)
Dot-myositis positive	88 (81.5)
Muscle biopsy	47 (43.9)

ANA: antinuclear antibodies; BMI: body mass index; NSIP: non specific interstitial pneumonia; NSJ: number of swollen joints; NSM: non specific microangiopathy; NTJ: number of tender joints; OP: organising pneumonia; PFT: pulmonary function test; SM: specific microangiopathy; UIP: usual interstitial pneumonia.

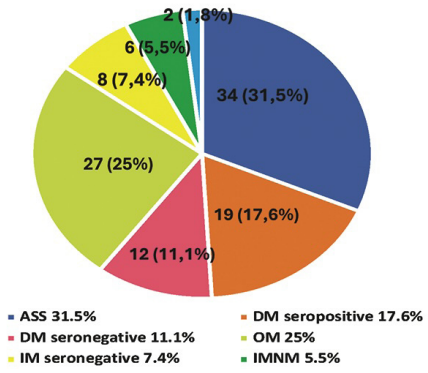


Fig. 1. Graphical population distribution into IM subgroups according to clinical signs and antibodies.

HAQ was <0.5: 81 (75%), 05<HAQ<1: 20 (18.5%), >1: 7 (6.5%). Skin showed DM lesions 72 (66.6%) and mechanic's hands 11 (10%). Respiratory symptoms concerned 66 (61.1%), 61 (59.8%) had ILD: 34 (51.5%) NSIP, 11 (16.6%) IUP (including 60% fibrosis) and 13 (19.7%) OP. Frequent associations of ≥1 HRCT pattern in the same patient such as NSIP/OP association in 9 (13.63%) found in ASS, PMScl-OM and MDA5-DM. General signs 36 (33.6%), sclerodactylitis 26 (24.1%), dry syndrome 61 (57%), calcinosis 6 (5.6%), and associated cancer in 3 (2.8%). ANA had speckled fluorescence 34 (41.5%), cytoplasmic 21 (27.27%), nucleolar 16 (20.77%), positive rheumatoid factor (RF) 11 (10.2%) and anti-citrullinated protein (ACPA) 8 (7.4%). Muscle biopsy revealed polymyositis 76 (70.2%), DM 4 (8.5%), inclusion body myositis 2 (1.9%). 99 (91.5%) were started on corticosteroids: 62 (62.24%) a dose of 0.5–1 mg/kg/day preceded by bolus in 16 (16.32%). Steroid withdrawal was possible in 44 (41.1%). Methotrexate was prescribed in half of the patients 53 (50%). They had already received: 45 (42.5%) hydroxychloroquine, 25 (23.6%) azathioprine, 21 (19.8%) cyclophosphamide, 18 (17%) MMF, 14 (13.2%) immunoglobulin, 5 (4.7%) anti-CD20 (rituximab), as tacrolimus is not available in Algeria; calcium channel blocker 47 (43.51%), 50 (47.6%) on wetting agents for dry syndrome and pneumococcal vaccination coverage was 87 (81.1%).

Clusters analysis

We used the same clustering model inspired by Mariamapillai *et al*. (3), a work carried out on 260 patients and by Palterer *et al*. (4) based on the new 2017 IM classification and on the ACR/EULAR criteria, to divide the population into clusters. We drew dendrograms using multiple correspondence analysis (MCA) and three clusters emerged (Fig. 2).

Cluster 1 (n=27) in green included patients with OM. This group was also characterised by the absence of several chronic pathologies such as diabetes, dyslipidaemia, and the use of immu-

nosuppressants, absence of worsening symptoms over time, dysphagia, arthritis and CK >225. On the other hand, this cluster contained very few men and few people with ASS. Cluster 2 (n=34) in red included ASS patients, mainly men (<50 years), smokers, with arthritis. It was also marked by an absence of hypertension and diabetes, and the presence of cytoplasmic ANA. Nevertheless, this cluster contained few people with OM. Cluster 3 (n=31) in purple included patients with DM, patients aged 50 years or older, a high proportion of hypertension, diabetes and dyslipidaemia, and immunosuppressant use. There was little arthritis or pulmonary hypertension. In addition, they had a CK level <225, a limitation of muscle strength (MMT8 ≤ 3) and typical skin involvement. These individuals tended to report a worsening of symptoms over time and encountered cases of dysphagia. This cluster had few people with OM.

Prognostic predictive factors

We used a binary logistic regression in ASS, then in the DM and the OM clusters to select variables whose *p*-value was <0.15 (univariate analysis). There were several predictive factors included for each subgroup. After regression (multivariate analysis), fewer variables were retained in the final model.

- Predictive factors of the ASS cluster

Patients receiving second-line IS were 4.30 times more likely to be in the ASS cluster compared with those not receiving this treatment, suggesting that this treatment was a specific ASS risk factor (OR=4.3; CI95% 1.55–12.49). Also, patients with positive cytoplasmic ANA were 4.44 times more likely to be in the ASS cluster compared with those with negative cytoplasmic ANA (OR=4 .4; CI95%1.64–12.61). This highlights that cytoplasmic ANA also represented a specific risk factor for this entity (Fig. 3). The area under the ROC curve validates the performance of the model and criterion estimated at 74.1%.

- Predictive factors of DM cluster

Patients with severe muscle strength limitation (MMT8 ≤3) had an odds ratio of 4.54, indicating that they are 4.54 times more likely to be classified in the DM cluster compared to those with minimal muscle limitation (OR=4.5; CI 95% 1, 58–14, 46). This indicated that this condition could be a specific prognostic factor for DM compared to other clusters (Fig. 4). The area under ROC curve validates the model performance and criterion estimated at 78.2%.

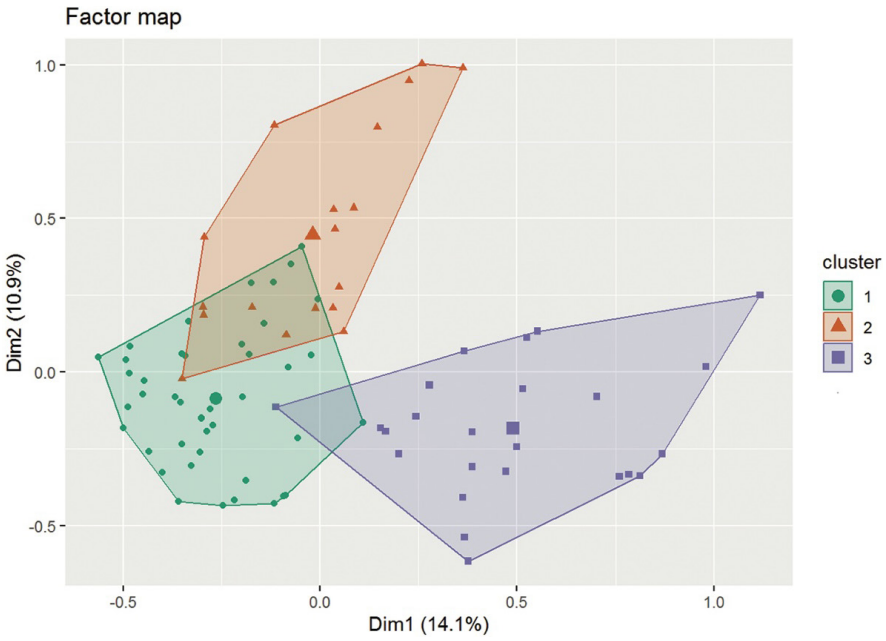
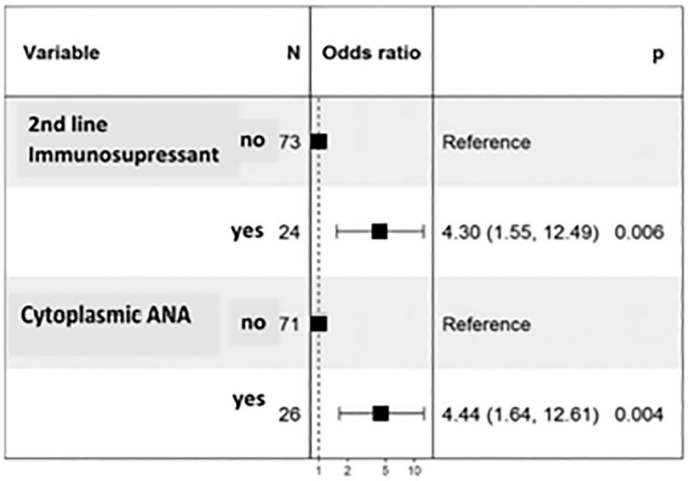


Fig. 2. Factor map of ascending hierarchical classification after dendrograms analysis.

Fig. 3. Forest plot of final model ASS prognostic factors.



- Predictive factors of the OM cluster

Patients with high blood pressure were 77% more likely to be classified in the OM cluster compared to those without high pressure. Patients with dysphagia were 3.5 times more likely to be in OM compared to those without dysphagia (OR=3.55; CI95%1.13–12.17). Furthermore, patients with a diagnostic delay >12 months were 3.4 times more likely to be in OM compared to those with a diagnostic delay ≤12 months, indicating that this characteristic could be a specific prognostic factor compared to other IM clusters (OR=3.41; CI95%1.17–10.32) (Fig. 5). The area under ROC curve validates the model performance and estimated criterion at 78.4%.

Analysis of small populations

Due to the small sample size, some subgroups could not be included in the cluster analysis but so as not to exclude them, we decided to describe them individually.

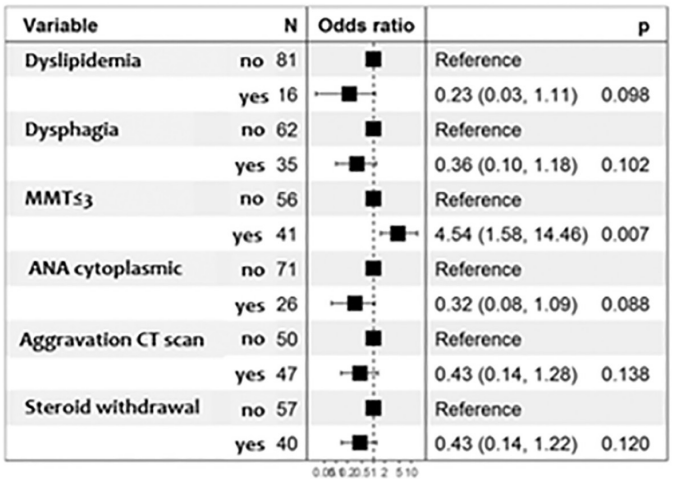


Fig. 4. Forest plot of final model DM prognostic factors.

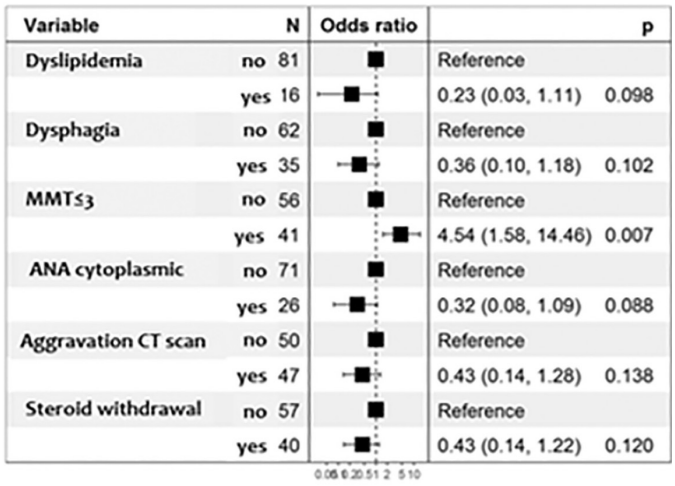


Fig. 5. Forest plot of final model OM prognostic factors.

- Group IMNM with signal recognition particles (SRP) (n=6)

Muscle involvement was severe (50% muscle testing ≤3) and they all had a biopsy showing positive HLA. Few had severe Raynaud's phenomenon, PID, dysphagia and arthritis. No patient had recourse to second-line IS. They responded well to methotrexate.

- Group IBM (n=2)

Two patients with significant proximal quadriceps deficit MMT8 ≤3 and hand flexor involvement, cN1A was positive in both patients. A biopsy of one of the patients found tissue degeneration with presence of typical inclusions. A patient followed the 'Sirolimus protocol' conducted by Benveniste O *et al*. in Paris, receiving rapamycin for 2 years which resulted in a slight improvement.

- IM seronegative (n=8)

Three (2.8%) cancers were found in this subgroup; most patients had elevated tumour markers, which would suggest investigating cancer in seronegative forms, and no patient received second-line treatment.

Discussion

Dhrif *et al*. (5) distinguished among several determinants in the univariate analysis, male sex factor as being predictive of ASS; we had found this same factor as predictive, CT worsening during follow-up and arthritis in the univariate. analysis However, the authors of the previous study had been able to isolate arthritis as predictive in the univariate analysis (RR=1.77, 95% CI 0.03–3.34 p=0.029). Similarly, Hervier *et al*. (6), had highlighted arthritis in the univariate analysis. In the multivariate analysis, our study made it possible to select cytoplasmic ANA fluorescence p < 0.004 and used second line immunosuppressants p<0.006. The same findings by Conrad *et al*. (7) specified that the speckled cytoplasmic fluorescence pattern is frequently associated with autoantibodies directed against cytoplasmic components such as anti-Jo-1. Moreover, in our study, the majority of the population with cytoplasmic ANA were Jo1 positive, while Hervier *et al*. (6) found ILD p<0.002, severe myolyses p<0.02, PHT p<0.05, ILD p<0.04 as predictive in ASS (8) and the same results were found by Marie *et al*. (9). In our study, muscle deficiency MMT8 ≤3 was predictive in DM. In a DM clinical trial Manseau *et al*. (10) reported that low muscle testing (MMT8 ≤3) represented the first prognostic factor, with cancer as the second one in the multivariate regression. Le Roux *et al*. (11) distinguished, in addition to having isolated dysphagia in the multivariate analysis, restrictive syndrome in PFT and myocarditis as prognosis factors in DM. On the other hand, after multivariate regression, high diagnostic delay emerged as predictive in the multivariate analysis in OM p=0.025, dysphagia was also found predictive after multivariate regression p=0.035. An international OM open trial conducted by Breillat *et al*. (12) found dysphagia factor to be predictive of OM (74.1 *vs*. 33.7% p=0.05). In the univariate analysis, Raynaud, PHT, and MMT8≤3 were significant in our study. Mastour *et al*. (13) reported dysphagia factor to be predictive in the univariate DM analysis, which was consistent with our results (p=0.007) of dysphagia in the univariate analysis.

As mentioned above, multiple correspondence analysis (MCA) was performed, taking into account all characteristics as well as prognostic factors, but could not take into account IBM, IMNM and seronegative myositis due to the lack of numbers within these subgroups.

The SRP-IMNM group of patients seemed to respond well to methotrexate (14). Seronegative IMs would seem to be associated with cancers (15), and the same finding was reported by Allenbach *et al*. (16). Le Roux *et al*. (11) found that the DM subgroup was associated with the highest mortality rate (12.5%), primarily due to cancer; anti-SAE1 an-

tibodies were associated with primarily ovarian and rectal cancers. The PL7 and PL12 subgroups were protective with the associated cancer variable.

At the end of this study, we proposed an algorithm that seemed to be useful for the diagnostic approach taught in continuing education courses for general practitioners, among others (Fig. 6).

The cause of myositis is not yet clearly established, but genetic and immunological factors, pollution, and the gut microbiota all contribute to the risk of onset and progression of the disease. Epigenetics explains how environmental factors (infections, UV radiation, stress) modify gene expression with/without altering DNA (17). These mechanisms promote chronic inflammation and attack muscle tissue. The exposome is now at the heart of research into these complex diseases and is central to prevention strategies, their progression, and the response to treatments. The coming decade places nutrition at the centre of research in terms of pathophysiology (18).

The main environmental mechanisms identified in these pathologies include: DNA methylation through chemical modifications to DNA that would hinder the activity of genes linked to the immune response through histone modifications; proteins around which DNA wraps are altered, facilitating access to pro-inflammatory genes; and finally, microRNAs (miRNAs) dysregulate the production of muscle and immune proteins, contributing to muscle weakness (17).

These discoveries pave the way for the identification of biomarkers through epigenetic profiles in blood or muscle biopsies, potentially enabling earlier and more accurate diagnosis as distinguishing dermatomyositis from IBM for example. They also contribute to the development of new therapies due to the reversible nature of epigenetic modifications aimed at switching off the genes responsible for inflammation (19).

Conclusion

IM subgroups have a rich clinical picture with a very heterogeneous phenotype. Antibodies are strongly associated with IM clinical and severity signs.

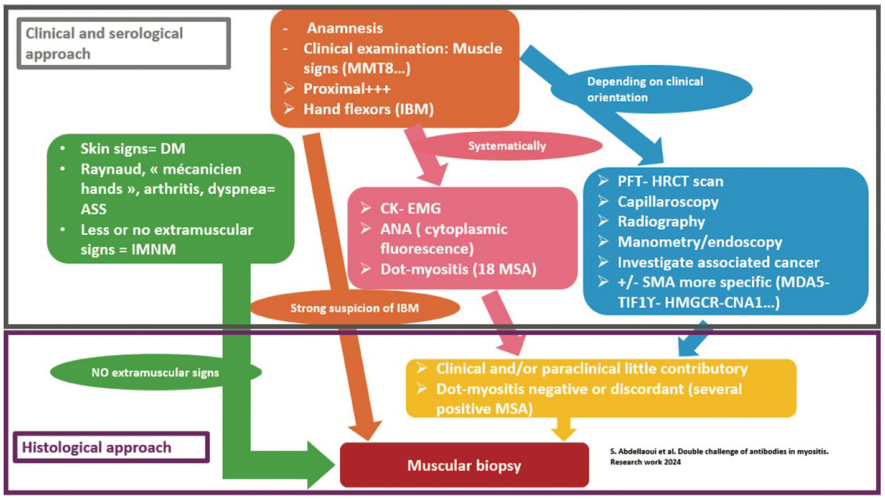


Fig. 6. Simplified algorithm of IM diagnostic approach.

This is the first Algerian IM cluster analysis allowed, through multidisciplinary meetings to collect 108 patients including some who felt a little left out and misunderstood, sometimes even ignorant of the name of their disease. We were able to divide our sample into three homogenous clusters, each cluster with fairly well-defined specific prognosis predictive factors.

References

1. LUNDBERG IE, TJÄRNLUND A, BOTTAI M *et al.*: 2017 European League Against Rheumatism/American College of Rheumatology classification criteria for adult and juvenile idiopathic inflammatory myopathies and their major subgroups. *Ann Rheum Dis* 2017; 76 (12): 1955-64. https://doi.org/10.1136/annrheumdis-2017-211468
2. OLDROYD A, CHINOY H: Recent developments in classification criteria and diagnosis guidelines for idiopathic inflammatory myopathies. *Curr Opin Rheumatol* 2018; 30(6) :606-13. https://doi.org/10.1097/bor.0000000000000549
3. MARIAMPILLAI K, GRANGER B, AMELIN D *et al.*: Development of a new classification system for idiopathic inflammatory myopathies based on clinical manifestations and myositis-specific autoantibodies. *JAMA Neurol* 2018; 75(12): 1528-37. https://doi.org/10.1001/jamaneurol.2018.2598
4. PALTERER B, VITIELLO G, CARRARESI A, GIUDIZI MG, CAMMELLI D, PARRONCHI P: Bench to bedside review of myositis autoantibodies. *Clin Mol Allergy* 2018; 7: 5. https://doi.org/10.1186/s12948-018-0084-9
5. DHRIF O, MEDDEB, KHALOUI ZM *et al.*: Influence of pulmonary involvement on the clinical, phenotypic and evolutionary presentation of idiopathic inflammatory myopathies. *Rev Med Intern* 2023; 44: A198-A265. https://doi.org/10.1016/j.revmed.2023.04.237
6. HERVIER B, TCHETGNIA L, CHAMPTIAUX N, BENVENISTE O, DEVILLIERS H: Qualitative study by individual interviews of the consequences of inflammatory myopathies on the quality of life. *Rev Med Intern* 2016; 37AS: A27-A88. https://doi.org/10.1016/j.revmed.2016.04.291
7. CONRAD K, SCHÖßLER W, HIEPE F, FRITZLER MJ (Eds.): Autoantibodies in Systemic Autoimmune Diseases PABST, Los Angeles, CA, USA. 2025.
8. JOSSE S, DECAUX O, DOMINIQUE S *et al.*: Idiopathic inflammatory myopathies and anti-PL7 or anti-PL12 antibodies. *Rev Med Intern* 2011; 32(S2): S258-S59. https://doi.org/10.1016/j.revmed.2011.10.289
9. MARIE I, DOMINIQUE S, HATRON PY *et al.*: Evolution and predictive factors of antisynthetase syndrome associated with anti-Ro52 antibodies. *Rev Med Intern* 2011; 32(S2): S252-S312. https://doi.org/10.1016/j.revmed.2011.10.290
10. MONSEAU G, LANDON-CARDINAL O, STENZEL W *et al.*: Systematic retrospective study of 64 patients with anti-Mi2 dermatomyositis: A classic skin rash with a necrotizing myositis and high risk of malignancy. *J Am Acad Dermatol* 2020; (83): 6. https://doi.org/10.1016/j.jaad.2020.03.058
11. LE ROUX A, SCHLEINITZ N, ATTARIAN S *et al.*: Long-term evolution and prognostic factors of idiopathic inflammatory myopathies, retrospective study of a regional cohort. *Rev Med Intern* 2021; 42: A28-A94. https://doi.org/10.1016/j.revmed.2021.03.317
12. BREILLAT P, MARIAMPILLAI K MARTINS P *et al.*: Spectre clinique et pronostic des connectivites à anti PM-Scl; une étude multicentrique incluant 128 patients. *Rev Med Intern* 2021; 42: A91-A92. https://doi.org/10.1016/j.revmed.2021.03.316
13. MASROUR H, FELK R, LERHRIB L *et al.*: Cardiac involvement in idiopathic inflammatory myopathies. *Rev Med Intern* 2023; 44: A198-A265. https://doi.org/10.1016/j.revmed.2023.04.259
14. PEYRE M, CHAMPTIAUX N, LANDON O *et al.*: Clinical presentation and evolutionary profile of autoimmune necrotizing myopathies with anti-SRP antibodies: French cohort of 54 patients. *Rev Med Intern* 2018; 39:

A23-A102. https://doi.org/10.1016/j.revmed.2018.10.344
15. ZAHR ZA, BAER AN: Malignancy in myositis. *Curr Rheumatol Rep* 2011; 13(3): 208-15. https://doi.org/10.1007/s11926-011-0169-7
16. ALLENBACH Y, KERAEN J, BOUVIER A-M *et al*.: High risk of cancer in autoimmune necrotizing myopathies: usefulness of myositis specific antibody. *Brain* 2016; 139: 2131-35. https://doi.org/10.1093/brain/aww054
17. OPINC-ROSIAK AH, MAKOWSKA JS: Environmental exposures as risk factors for idiopathic inflammatory myopathies. *J Autoimmun* 2023; 140: 103095. https://doi.org/10.1016/j.jaut.2023.103095
18. CARDELLI C, TRENTIN F, FATTORINI F *et al*.: Environmental triggers for idiopathic inflammatory myopathies: unravelling the known and unknown. *Clin Exp Rheumatol* 2025; 43(2): 186-92. https://doi.org/10.55563/clinexprheumatol/0x1gob
19. PALTERER B, MAZZONI A, INFANTINO M *et al*.: Seasonal patterns of myositis-specific and myositis-associated autoantibodies in Italy: Seasonal patterns of myositis autoantibodies. *Immunol Lett* 2025; 272: 106966. https://doi.org/10.1016/j.imlet.2024.106966